

# Exhibit 6

<b>Notice of Allowability</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/380,696	LO ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Jeanine A Enewold Goldberg	1655	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance and Issue Fee Due or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 12/27/00; 1/11/01; 1/16/01.

2. ☒ The allowed claim(s) is/are 1 and 3-28.

3. ☐ The drawings filed on \_\_\_\_\_ are acceptable as formal drawings.

4. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All    b) ☐ Some\*    c) ☐ None    of the:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_

3. ☒ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_

5. ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. **THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

6. ☐ Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient. A SUBSTITUTE OATH OR DECLARATION IS REQUIRED.

7. ☒ Applicant MUST submit NEW FORMAL DRAWINGS

(a) ☒ including changes required by the Notice of Draftsperson's Patent Drawing Review( PTO-948) attached

1) ☐ hereto or 2) ☒ to Paper No. 9.

(b) ☐ including changes required by the proposed drawing correction filed \_\_\_\_\_, which has been approved by the examiner.

(c) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No. \_\_\_\_\_

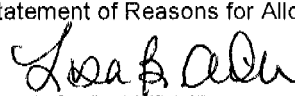
**Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.**

8. ☐ Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Any reply to this letter should include, in the upper right hand corner, the APPLICATION NUMBER (SERIES CODE / SERIAL NUMBER). If applicant has received a Notice of Allowance and Issue Fee Due, the ISSUE BATCH NUMBER and DATE of the NOTICE OF ALLOWANCE should also be included.

**Attachment(s)**

<p>1 <input type="checkbox"/> Notice of References Cited (PTO-892)</p> <p>3 <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)</p> <p>5 <input type="checkbox"/> Information Disclosure Statements (PTO-1449), Paper No. _____</p> <p>7 <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit of Biological Material</p>	<p>2 <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)</p> <p>4 <input checked="" type="checkbox"/> Interview Summary (PTO-413), Paper No. <u>14.</u></p> <p>6 <input checked="" type="checkbox"/> Examiner's Amendment/Comment</p> <p>8 <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance</p> <p>9 <input type="checkbox"/> Other</p>
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**LISA B. ARTHUR**  
**PRIMARY EXAMINER**  
**GROUP 1800-1600**

Application/Control Number: 09/380,696  
Art Unit: 1655

17/F  
Page 2  
JY  
1/23/01

### EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Frederick Koenig on January 16, 2001.

2. The application has been amended as follows:

F<sub>1</sub>  
1. (Twice Amended) A [nucleic acid detection] method for detecting a paternally inherited nucleic acid of fetal origin performed on a maternal serum or plasma sample from a pregnant female, which method comprises amplifying a paternally inherited nucleic acid from the serum or plasma sample and detecting the presence of a paternally inherited nucleic acid of fetal origin in the sample.

Cancel Claim 2.

F<sub>2</sub>  
23. The method according to Claim [2] 1, wherein the foetal nucleic acid is amplified by the polymerase chain reaction.

[ In Claim 4, "2" has been amended to -- 1 --.

F<sub>3</sub>  
25. (Amended) A method for detecting a paternally inherited nucleic acid [ of performing a prenatal diagnosis] on a maternal blood sample, which method comprises: removing all or substantially all nucleated and anucleated cell populations from the blood sample, amplifying a paternally inherited nucleic acid from the remaining fluid and subjecting the amplified nucleic acid [remaining fluid] to a test for the paternally inherited fetal nucleic acid [indicative of a maternal or fetal condition or characteristic] .

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F<sub>4</sub> 26. (Twice Amended) A method for performing a prenatal diagnosis on a maternal blood sample, which method comprises  
obtaining a non-cellular fraction of the blood sample  
amplifying a paternally inherited nucleic acid from the non-cellular fraction  
and performing nucleic acid analysis on the [fraction] amplified nucleic acid to detect paternally inherited fetal nucleic acid.

The first line of the specification has been amended to insert -- This application

F<sub>5</sub> is the national stage of PCT Application No. PCT/GB98/00690, filed March 4, 1998  
under 37 CFR 371) --

3. The following is an examiner's statement of reasons for allowance.

The claims are drawn to a method of detecting paternally inherited nucleic acid of fetal origin performed on a maternal serum or plasma sample from a pregnant female, by amplifying a paternally inherited nucleic acid from the serum or plasma sample and detecting the presence of a paternally inherited nucleic acid of fetal origin in the sample.

The closest prior art is directed to detecting alterations in plasma DNA for diagnosing and or monitoring the development of DNA (Stroun et al GB 2299166, September 1996). The art also teaches detecting fetal cells in maternal blood and performing diagnostic tests on the blood. However, the art does not teach nor reasonably suggest that nucleic acid of fetal origin is present in maternal serum or plasma.

4. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably

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accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Enewold Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Thursday from 7:00AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jeanine Enewold Goldberg  
January 23, 2001 *JS*

*Lisa B. Arthur*  
LISA B. ARTHUR  
PRIMARY EXAMINER  
GROUP 1800-1600

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<b>Interview Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/380,696	LO ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Jeanine A Enewold Goldberg	1655	

All participants (applicant, applicant's representative, PTO personnel):

(1) Jeanine A Enewold Goldberg. (3) \_\_\_\_\_.

(2) Frederick Koenig. (4) \_\_\_\_\_.

Date of Interview: 11 January 2001.

Type: a) ☒ Telephonic b) ☐ Video Conference  
c) ☐ Personal [copy given to: 1) ☐ applicant 2) ☐ applicant's representative]

Exhibit shown or demonstration conducted: d) ☐ Yes e) ☐ No.

If Yes, brief description:

Claim(s) discussed: \_\_\_\_\_.

Identification of prior art discussed:

Agreement with respect to the claims f) ☐ was reached. g) ☐ was not reached. h) ☐ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: The examiner called to discuss the after final amendment. While the applicants have provided the necessary changes, the examiner upon further consideration believes that an amplification step is a necessity for the claimed invention. The examiner indicated that prosecution would be reopened.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

i) ☐ It is not necessary for applicant to provide a separate record of the substance of the interview (if box is checked).

Unless the paragraph above has been checked, THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN ONE MONTH FROM THIS INTERVIEW DATE TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

J. Goldberg  
Examiner's signature, if required

UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office

## NOTICE OF ALLOWANCE AND ISSUE FEE DUE

HM32/0301

C FREDERICK KOENIG III  
VOLPE & KOENIG  
400 ONE PENN CENTER  
1617 JOHN F KENNEDY BOULEVARD  
PHILADELPHIA PA 19103

APPLICATION NO.	FILING DATE	TOTAL CLAIMS	EXAMINER AND GROUP ART UNIT	DATE MAILED
09/380,696	11/29/99	027	GOLDBERG, J 1655	03/01/01
First Named Applicant	LO, 35 USC 154(b) term ext. = 0 Days.			

TITLE OF INVENTION NON-INVASIVE PRENATAL DIAGNOSIS

ATTY'S DOCKET NO.	CLASS-SUBCLASS	BATCH NO.	APPLN. TYPE	SMALL ENTITY	FEE DUE	DATE DUE
1 SHP-PT048	435-006,000	C86	UTILITY	NO	\$1240.00	06/01/01

**THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED.**

**THE ISSUE FEE MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED.**

**HOW TO RESPOND TO THIS NOTICE:****I. Review the SMALL ENTITY status shown above.**

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

If the SMALL ENTITY is shown as NO:

A. If the status is changed, pay twice the amount of the FEE DUE shown above and notify the Patent and Trademark Office of the change in status, or

A. Pay FEE DUE shown above, or

B. If the status is the same, pay the FEE DUE shown above.

B. File verified statement of Small Entity Status before, or with, payment of 1/2 the FEE DUE shown above.

II. Part B-Issue Fee Transmittal should be completed and returned to the Patent and Trademark Office (PTO) with your ISSUE FEE. Even if the ISSUE FEE has already been paid by charge to deposit account, Part B Issue Fee Transmittal should be completed and returned. If you are charging the ISSUE FEE to your deposit account, section "4b" of Part B-Issue Fee Transmittal should be completed and an extra copy of the form should be submitted.

III. All communications regarding this application must give application number and batch number. Please direct all communications prior to issuance to Box ISSUE FEE unless advised to the contrary.

**IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.**

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